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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,336	04/26/2007	Claudia Woppmann	051058-1000	2542

84717 7590 04/01/2009

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EXAMINER	
ZARA, JANE J	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,336	WOPPMANN ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-74* is/are pending in the application.

4a) Of the above claim(s) *57-69 and 71-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-56 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-18-08,8-7-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 1-15-09.

Claims 44-74 are pending in the application.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Please provide support for SEQ ID NOs. 27-30 in the priority documents. Support for these sequences could not found in the foreign priority documents.

Election/Restrictions

Applicant's election with traverse of Group I, claim 2, and the SEQ ID No. represented by P4 (example 6, page 88, SEQ ID NOs. 46 and 47 as self complementary strands of an siRNA molecule) in the reply filed on 1-15-09 is acknowledged. The traversal is on the ground(s) that no serious burden has been shown to examine all the groups together. This is not found fully persuasive because the claims read broadly on a myriad of sequences and a proper examination of all of the

sequence encompassed by the claims would indeed pose a serious burden on the Examiner and the USPTO facilities.

Applicant also argues that the methods claims, claims 71-74 should also be examined because they depend from an elected claim. As set forth in the restriction requirement of record, the Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejections are governed by 37 CFR 1.116; amendments submitted after allowances are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March

26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement is still deemed proper and is therefore made FINAL.

Claims 57-69, 71-74, and SEQ ID Nos. **other than SEQ ID Nos. 46 and 47**, represented by P4 on page 88 of the instant specification, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1-15-09.

Accordingly, claims 44-56, and 70, and SEQ P4 (an siRNA molecule comprising SEQ ID Nos. 46 and 47) have been examined on their merits as set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-56, and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "the terminal base of the first double-stranded end" (see line 11 of claim 44) and "the terminal base pair of the second double-stranded end" (see, e.g., lines 12-13 of claim 44). It is unclear to which termini the claims are referring.

Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-56, and 70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to compositions, including pharmaceutical compositions comprising any RNAi molecule consisting of first and second single RNA strands, which first strand is antisense to a target gene and is 19-28 bases in length, and which RNAi molecule further comprises at least one single-stranded overhang that is 2-4 nucleotides in length, which unpaired nucleotide of the overhang is adjacent to a terminal pair of purine bases, or half of the unpaired nucleotides are purine bases, and the 3'-end of the antisense strand comprises an overhang of 5'-GC-3', and the terminal base pair of the first double stranded end comprises a G-C base pair or two G-C base pairs, wherein the terminal base pair of the first or second double stranded ends

comprise a G-C base pair or the four consecutive terminal base pairs of the second double stranded end comprises at least two G-C base pairs, and excluding RNAi molecules consisting of SEQ ID Nos. ! and 2, 27 and 28, or 29 and 30, and which RNAi molecules optionally further comprise 2'-O-alkyl, amino or 2'-deoxy-2'-fluoro modifications.

The specification and claims do not adequately describe a representative number of species for this expansive genus of molecules claimed, and which provide for the functions claimed, of having increased effectiveness in inhibiting the expression of any target gene, or of having any treatment effects in a subject. The specification teaches some specific RNAi sequences in tables 1, 2, and 3 (pages 13-16 of the specification). The specification also teaches in vitro, serum stability of some specific RNAi sequences (pages 87-88) and in vitro melting temperature (Tm) determinations for a subset of RNAi sequences. The examples provided, however, do not provide adequate representation of the very broad genus of compounds claimed (which genus encompasses thousands and thousands of sequences).

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus claimed, or which provide for the functions claimed, of having increased effectiveness in inhibiting the expression of any target gene, or of having any treatment effects in a subject. Thus, Applicant was not in possession of the broadly claimed genus. One of skill in the art would therefore reasonably conclude that adequate written description is lacking for the instantly claimed, and very broad genus of inhibitory compounds claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 44-56, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tuschl et al (WO/ 02/44321) in view of Tolentino et al (USPN 7,345,027) insofar as the claims are drawn to compositions comprising an RNAi molecule consisting of first and second single RNA strands, which first strand is antisense to a target gene and is 19-28 bases in length, and which RNAi molecule further comprises at least one single-stranded overhang that is 2-4 nucleotides in length, which unpaired nucleotide of the overhang is adjacent to a terminal pair of purine bases, or half of the unpaired nucleotides are purine bases, and the 3'-end of the antisense strand comprises an overhang of 5'-GC-3', and the terminal base pair of the first double stranded end

comprises a G-C base pair or two G-C base pairs, wherein the terminal base pair of the first or second double stranded ends comprise a G-C base pair or the four consecutive terminal base pairs of the second double stranded end comprises at least two G-C base pairs, and which RNAi molecules optionally further comprise 2'-O-alkyl, amino or 2'-deoxy-2'-fluoro modifications.

Tuschl et al (WO/ 02/44321) teach compositions comprising an RNAi molecule consisting of first and second single RNA strands, which first strand is antisense to a target gene and is 19-28 bases in length, and which RNAi molecule further comprises at least one single-stranded overhang that is 2-4 nucleotides in length. Tuschl teaches routine experimental approaches to systematically compare the stability and target gene inhibiting capacity of RNAi molecules, including comparing an array of different overhangs, of different lengths between 1-4 nucleotides, for enhancing stability and target gene inhibition. Tuschl also teaches the incorporation of 2'O-alkyl and 2'-deoxy modifications, and phosphorothioate internucleotide linkages into RNAi molecules, and the effect of these modifications on RNAi stability, target binding and target gene inhibition (see entire document, esp. the abstract, pages 43-48; figures 7, 8, 11, 16-23, claims 1-16).

Tuschl does not teach the location of purine residues with respect to RNAi overhangs and adjacent nucleobase sequences.

Tolentino et al (USPN 7,345,027) teach the design, testing and optimization of RNAi molecules in their ability to inhibit target gene expression. Tolentino teaches RNAi molecules with 3' overhangs on one or both strands between 1-6 bases,

preferably 1-4 nucleobases, the importance of the location of purines and modified residues on the RNAi strands, and the testing of these RNAi molecules for enhanced stability and target gene binding and inhibition of expression (see esp. col. 4-6).

It would have been obvious to design RNAi molecules between 19-28 bases which comprises target sequence that is complementary to a known gene sequence, and comprising the overhangs and modifications as instantly claimed because it was well known in the art at the time of the instant invention that RNAi molecules of this size range, and comprising overhangs of this size range are most stable from degradation, and optimally inhibit expression of a known target gene. One would have been motivated to alter the bases and insert purines at the positions within the RNAi as instantly claimed because both Tolentino and Tuschl teach methods of optimizing overhangs, and of optimizing the location of modified residues to produce the most efficient and most stable RNAi molecules for target gene inhibition, and to do so involved routine experimentation at the time of the instant invention. One would have been motivated to place overhangs as instantly claimed onto the 3' ends of the RNAi molecule because Tolentino teaches that these overhangs enhance stability, and both Tolentino and Tuschl identify the regions and strands of the RNAi molecule that are involved in target gene recognition, guidance, and target gene inactivation. One of skill in the art would have reasonably expected that the instantly claimed RNAi molecules would provide for enhanced stability and target gene inhibition, the placements of the modifications and bases onto the overhangs would have been a matter of design

choice, and identifying the optimal RNAi molecules would have involved routine experimentation at the time of the instant invention.

For these reasons, the instant invention would have been obvious to one of skill in the art at the time of filing.

Allowable Subject Matter

The RNAi molecule consisting of the self-complementary strands, SEQ ID NO. 46 and SEQ ID NO. 47, appears free of the prior art searched and of record.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of

a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
3-25-09

/Jane Zara/

Primary Examiner, Art Unit 1635